

REHM
Appl. No. 10/525,955
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AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-29 (cancelled).

30 (withdrawn). A process for the production of biodegradable polymer particles which comprises:

a) introduction of at least one inducible gene into a microorganism, wherein the gene codes for a protein which controls the size of the polymer particles and is selected from the group which comprises the phasin gene phaP from *Ralstonia eutropha* and the phasin gene phaF from *Pseudomonas oleovorans*;

b) introduction of at least one further gene which codes for a protein involved in the formation of the polymer particles;

wherein at least one of the genes introduced into the microorganism in a) and b) comprises a polymer particle binding domain and at least one binding domain, wherein the at least one binding domain is capable of binding a biologically active substance and/or a coupling reagent; and

c) cultivation of the microorganism with induction of the at least one inducible gene stated in a) in a culture medium under conditions which are suitable for the production of the biodegradable polymer particles by the microorganism.

REHM
Appl. No. 10/525,955
April 14, 2008

31 (withdrawn). A process according to claim 30, wherein the at least one further gene which codes for a protein involved in the formation of the polymer particles codes for a thiolase, a reductase or a polymer synthase.

32 (withdrawn). A process according to claim 31, wherein the at least one further gene which codes for a protein involved in the formation of the polymer particles codes for phaA thiolase, phaB ketoacyl reductase or phaC synthase from *Ralstonia eutropha*.

33 (withdrawn). A process according to claim 30, wherein at least one additional gene which codes for a thiolase and/or a polymer synthase is introduced into the cell.

34 (withdrawn). A process according to claim 30, wherein at least one fatty acid with functional side groups and particularly preferably at least one hydroxy fatty acid and/or at least one mercapto fatty acid and/or at least one β -amino fatty acid is introduced into the culture medium as a substrate for the formation of the polymer particles.

35 (withdrawn). A process according to claim 30, wherein a substrate is added to the culture medium in such a quantity that it is sufficient to ensure control of the size of the polymer particles.

REHM

Appl. No. 10/525,955

April 14, 2008

36 (withdrawn). A process according to claim 30, wherein the microorganism used is selected from the genera comprising *Ralstonia*, *Alcaligenes*, *Pseudomonas* and *Halobiforma*.

37 (withdrawn). A process according to claim 36, wherein the microorganism used is selected from the group comprising *Ralstonia eutropha*, *Alcaligenes latus*, *Escherichia coli*, *Pseudomonas fragi*, *Pseudomonas putida*, *Pseudomonas oleovorans*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, and *Halobiforma haloterrestris*.

38 (withdrawn). A process according to claim 30, wherein the cultivated microorganisms are disrupted in per se known manner and the polymer particles then separated from the cell debris.

39 (withdrawn). A process according to claim 38, wherein a lipid layer located on the surface of the polymer particles is separated from the polymer particles obtained according to the process of claim 38 and replaced by a lipid layer of another composition.

40 (withdrawn). A process according to claim 30, wherein particle size is controlled by the at least one inducible gene in such a manner that the polymer particles formed have a diameter of 10 nm to 3 μ m, preferably a diameter of 10 nm to 900 nm, and particularly preferably a diameter of 10 nm to 100 nm.

REHM
Appl. No. 10/525,955
April 14, 2008

41 (withdrawn). A process according to claim 30, wherein the polymer particle binding domain comprises part of a protein bound to the surface of the polymer particle, wherein the protein is selected from the group comprising a polymer depolymerase, a polymer regulator, a polymer synthase and a particle size-controlling protein.

42 (withdrawn). A process according to claim 30, wherein the at least one binding domain which is capable of binding a biologically active substance and/or a coupling reagent is selected from the group comprising oligopeptides, enzymes, abzymes or non-catalytic proteins.

43 (withdrawn). A process for the *in vitro* production of biodegradable polymer particles consisting of polyhydroxyalkyl carboxylates which comprises:

- a) provision of a solution suited to polymer particle formation with at least one substrate;
- b) introduction into the solution of a protein which is suited to controlling the size of the polymer particles; and
- c) introduction of at least one further protein which is involved in the formation of the polymer particles,

wherein at least one of the proteins introduced in stage b) and/or c) is selected such that it comprises a polymer particle binding domain and at least one binding domain, wherein the at least one binding domain is capable of binding a biologically active substance and/or a coupling reagent.

REHM
Appl. No. 10/525,955
April 14, 2008

44 (withdrawn). A process according to claim 43, wherein at least one fatty acid and an acyl CoA oxidase is added to the solution suited to polymer particle formation in stage a).

45 (withdrawn). A process according to claim 43, wherein, in stage a), at least one substrate is added to the solution suited to polymer particle formation in such quantity that it is sufficient to ensure control of the size of the polymer particles.

46 (withdrawn). A process according to claim 43, wherein, in stage b), a polymer particle size-controlling protein is introduced which is derived from the family of phasin-like proteins.

47 (withdrawn). A process according to claim 46, wherein, in stage b), a polymer particle size-controlling protein is introduced which is selected from the group comprising the phasin from *Ralstonia eutropha* and the phasin from *Pseudomonas oleovorans*.

48 (withdrawn). A process according to claim 43, wherein the at least one further protein involved in polymer particle formation used in stage c) is a polymer synthase.

REHM
Appl. No. 10/525,955
April 14, 2008

49 (withdrawn). A process according to claim 48, wherein the at least one further protein involved in polymer particle formation used in stage c) is a polymer synthase which is selected from the group comprising the polymer synthase from *R. eutropha*, *P. oleovorans*, *P. putida* and *P. aeruginosa*.

50 (withdrawn). A process according to claim 48, wherein the polymer synthase is added to the solution in such a quantity that it is sufficient to ensure control of the size of the polymer particles.

51 (withdrawn). A process according to claim 43, wherein, in stage a), at least one pharmaceutically active substance is added to the solution.

52 (withdrawn). A process according to claim 43, wherein, in order to control the composition of the lipid layer on the surface of the polymer particle, at least one amphiphilic molecule from the group of phospholipids and ether lipids is added to the solution from step a).

53 (withdrawn). A process according to claim 43, wherein the polymer particle binding domain is part of the protein bound to the surface of the polymer particle, wherein the protein is selected from the group which comprising a polymer depolymerase, a polymer regulator, a polymer synthase and a particle size-controlling protein.

REHM

Appl. No. 10/525,955

April 14, 2008

54 (withdrawn). A process according to claim 43, wherein the at least one binding domain which is capable of binding a biologically active substance and/or a coupling reagent is selected from the group comprising oligopeptides, enzymes, abzymes or non-catalytic proteins.

55 (withdrawn). A polymer particle of polyhydroxyalkyl carboxylates of defined size comprising a surface layer of amphiphilic molecules and at least one protein which is selected from the group comprising a polymer depolymerase, a polymer regulator, a polymer synthase and a particle size-influencing protein, wherein the at least one protein comprises a polymer particle binding domain and a binding domain which is capable of binding a biologically active substance and/or a coupling reagent.

56 (withdrawn). A polymer particle of polyhydroxyalkyl carboxylates of defined size comprising a surface layer of amphiphilic molecules and at least one protein which is selected from the group comprising a polymer depolymerase, a polymer regulator, a polymer synthase and a particle size-influencing protein, wherein the at least one protein comprises a polymer particle binding domain and a binding domain which is capable of binding a biologically active substance and/or a coupling reagent, and wherein the polymer particle is produced according to a process as defined in claim 30.

57 (withdrawn). A pharmaceutical preparation, a pesticide or a herbicide comprising a polymer particle according to claim 55.

REHM
Appl. No. 10/525,955
April 14, 2008

58 (withdrawn): A method for treating or preventing a disease of the central nervous system comprising administering a polymer particle of claim 54 to a subject in need thereof.

59 (currently amended). A process for producing ~~polymer~~ polyhydroxy carboxylate particles having surface-bound proteins, the process comprising:

A) providing a cell comprising:

~~(1) at least one gene that codes for a polymer synthase, the polymer synthase comprising a polymer particle binding domain; or~~

~~(2) at least one gene that codes for a fusion protein, the fusion protein comprising a polymer synthase and~~

~~(a) at least one binding domain capable of binding one or more biologically active substances or one or more coupling reagents or a combination thereof, or~~

~~(b) at least one biologically active protein, or~~

~~(c) a combination thereof,~~

fused with the N-terminus of the polymer synthase, the polymer synthase of the ~~fusion protein~~ comprising a polymer particle binding domain; and

~~(3) optionally~~

~~(a) at least one gene that codes for a protein involved in the formation of polymer particles, the protein comprising a polymer particle binding domain; or~~

~~(b) at least one gene that codes for an additional fusion protein, the additional fusion protein comprising~~

REHM
Appl. No. 10/525,955
April 14, 2008

~~(i) a polymer particle binding domain or a protein involved in the formation of the polymer particles, the protein comprising a polymer particle binding domain, or a combination thereof, and~~

~~(ii) at least one biologically active protein or at least one binding domain capable of binding one or more biologically active substances or one or more coupling reagents or a combination thereof, or~~

~~(iii) at least one biologically active protein and at least one binding domain capable of binding one or more biologically active substances or one or more coupling reagents or a combination thereof, or~~

~~(e) a combination thereof;~~

B) cultivating the cell in a culture medium so that the cell produces an expression product the fusion protein from the at least one gene and produces polymer particles comprising polyhydroxy carboxylate, wherein the polymer particle binding domain of the expression product fusion protein is bound to a polymer particle; and

C) separating the polymer particles from the cultivated cells to produce a composition comprising polymer polyhydroxy carboxylate particles having surface-bound proteins.

60 (currently amended). A process according to claim ~~59~~ 100, wherein the at least one gene that codes for a protein involved in the formation of polymer particles is selected from the group consisting of a gene coding for a phaA thiolase, a gene coding for a phaB ketoacyl reductase, a gene coding for a polymer depolymerase, a gene

REHM
Appl. No. 10/525,955
April 14, 2008

coding for a polymer regulator, a gene coding for a polymer synthase and a gene coding for a particle size-determining protein or a combination thereof.

61 (withdrawn). A process according to claim 60, wherein the particle size-determining protein is a phasin.

62 (withdrawn). A process according to claim 60, wherein the polymer regulator is phaR.

63 (withdrawn). A process according to claim 60, wherein the polymer depolymerase, polymer regulator, polymer synthase or particle size-determining protein is from a microorganism of the genera *Ralstonia*, *Alcaligenes* or *Pseudomonas*.

64 (previously presented). A process according to claim 59, wherein the polymer synthase is from *Ralstonia eutropha*, *Pseudomonas oleovorans*, *Pseudomonas putida*, *Pseudomonas aeruginosa*, *Aeromonas punctata* or *Thiocapsa pfennigii*.

65 (withdrawn). A process according to claim 61, wherein the phasin is phaP from *Ralstonia eutropha* or phaF or phaI from *Pseudomonas oleovorans*.

66 (withdrawn). A process according to claim 59, wherein the polymer particle binding domain comprises the particle binding domain of a protein selected from

REHM
Appl. No. 10/525,955
April 14, 2008

the group consisting of a polymer depolymerase, a polymer regulator, a polymer synthase and a particle size-determining protein.

67 (withdrawn). A process according to claim 66, wherein the particle size-determining protein is a phasin.

68 (withdrawn). A process according to claim 66, wherein the polymer regulator is phaR.

69 (withdrawn). A process according to claim 66, wherein the polymer depolymerase, polymer regulator, polymer synthase or particle size-determining protein is from a microorganism of the genera *Ralstonia*, *Alcaligenes* or *Pseudomonas*.

70 (withdrawn). A process according to claim 66, wherein the polymer synthase is from *Ralstonia eutropha*, *Pseudomonas oleovorans*, *Pseudomonas putida*, *Pseudomonas aeruginosa*, *Aeromonas punctata* or *Thiocapsa pfennigii*.

71 (withdrawn). A process according to claim 67, wherein the phasin is phaP from *Ralstonia eutropha* or phaF or phal from *Pseudomonas oleovorans*.

72 (previously presented). A process according to claim 59, wherein the culture medium comprises at least one fatty acid with a functional side group selected from methyl groups, alkyl groups, hydroxyl groups, phenyl groups, sulfhydryl groups, primary,

REHM
Appl. No. 10/525,955
April 14, 2008

secondary and tertiary amino groups, aldehyde groups, keto groups, ether groups, carboxyl groups, O-ester groups, thioester groups, carboxylic acid amide groups, hemiacetal groups, acetal groups, phosphate monoester groups and phosphate diester groups, or a mixture of any two or more thereof.

73 (previously presented). A process according to claim 59, wherein a substrate is added to the culture medium in such a quantity that it is sufficient to ensure control of the size of the polymer particles.

74 (previously presented). A process according to claim 59, wherein the cell is a microorganism selected from

- a) the genera consisting of *Escherichia*, *Ralstonia*, *Alcaligenes*, *Pseudomonas* and *Halobiforma*; or
- b) the group consisting of *Ralstonia eutropha*, *Alcaligenes latus*, *Escherichia coli*, *Pseudomonas fragi*, *Pseudomonas putida*, *Pseudomonas oleovorans*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens* and *Halobiforma haloterrestis*.

75 (previously presented). A process according to claim 59, wherein a lipid layer located on the surface of the polymer particles is separated from the polymer particles and replaced by a lipid layer of another composition.

76 (previously presented). A process according to claim 59, wherein the polymer particles have a diameter of 10 nm to 3 μ m.

REHM
Appl. No. 10/525,955
April 14, 2008

77 (previously presented). A process according to claim 59, wherein the polymer particles have a diameter of 10 nm to 900 nm.

78 (previously presented). A process according to claim 59, wherein the polymer particles have a diameter of 10 nm to 100 nm.

79 (previously presented). A process according to claim 59, wherein at least one biologically active substance or at least one dye or a mixture thereof is added to the culture medium and incorporated into the particles.

80 (previously presented). A process according to claim 59, wherein the at least one binding domain is selected from the group consisting of one or more oligopeptides, one or more enzymes, one or more abzymes, one or more non-catalytic proteins, one or more FLAG epitopes and one or more one cysteine residues or a combination thereof.

81 (currently amended). A process according to claim ~~60~~ 59, wherein the polymer synthase is bound to the polymer particle by a covalent bond.

82 (previously presented). A process according to claim 59, further comprising
D) binding a coupling reagent to the binding domain.

83 (previously presented). A process according to claim 59, further comprising

REHM

Appl. No. 10/525,955

April 14, 2008

- D) binding a coupling reagent to the binding domain; and
- E) binding a biologically active substance to the coupling reagent.

84 (previously presented). A process according to claim 59, further comprising

- D) binding a biologically active substance to the binding domain.

85 (previously presented). A process according to claim 59, further comprising

- D) chemically modifying the polymer synthase or the protein involved in the formation of polymer particles to form at least one binding domain by contacting the polymer synthase or the protein with a coupling reagent.

86 (previously presented). A process according to claim 59, wherein the biologically active substance is able to bind another biologically active substance.

87 (previously presented). A process according to claim 59, wherein the biologically active substance comprises a pharmaceutically active substance.

88 (previously presented). A process according to claim 59, wherein the biologically active substance is selected from

- A) dideoxyinosine, floxuridine, 6-mercaptopurine, doxorubicin, daunorubicin, 1-darubicin, cisplatin, methotrexate, taxol, antibiotics, anticoagulants, germicides, antiarrhythmic agents and active ingredient precursors or derivatives thereof, or

REHM
Appl. No. 10/525,955
April 14, 2008

B) Insulin, calcitonin, ACTH, glucagons, somatostatin, somatotropin, somatomedin, parathyroid hormone, erythropoietin, hypothalamic release factors, prolactin, thyroid-stimulating hormone, endorphins, enkephalins, vasopressins, non-naturally occurring opiates, superoxide dismutase, antibodies, interferons, asparaginase, arginase, arginine deaminase, adenosine deaminase, ribonuclease, trypsin, chymotrypsin or pepsin.

89 (previously presented). A process according to claim 59, wherein the biologically active protein is selected from insulin, calcitonin, ACTH, glucagons, somatostatin, somatotropin, somatomedin, parathyroid hormone, erythropoietin, hypothalamic release factors, prolactin, thyroid-stimulating hormone, endorphins, enkephalins, vasopressins, non-naturally occurring opiates, superoxide dismutase, antibodies, interferons, asparaginase, arginase, arginine deaminase, adenosine deaminase, ribonuclease, trypsin, chymotrypsin or pepsin.

90 (previously presented). A process according to claim 59, wherein the biologically active substance or the biologically active protein is an antibody or antibody fragment.

91 (previously presented). A process according to claim 85, wherein the coupling reagent is selected from the group consisting of bis(2-oxo-3-oxazolidinyl)phosphonic chloride (BOP-Cl), bromotrispyrrolidinophosphonium hexafluorophosphate (PyBroP), benzotriazol-1-yl-oxy-trispyrrolidinophosphonium hexafluorophosphate (PyBOP), n-

REHM

Appl. No. 10/525,955

April 14, 2008

hydroxysuccinimide biotin, 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), dicyclohexylcarbodiimide, disuccinimidyl carbonate, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC), bis(2-oxo-3-oxazolydinyl)phosphine, diisopropylcarbodiimide (DIPC), 2-(1H-benzotrioxazolyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(5-norbornene-2,3-dicarboxyimido)-1,1,3,3-tetramethyluronium tetrafluoroborate (TNTU), para-nitrophenylchloroformate, and O-(n-succinimidyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TSTU).

92 (previously presented). A process according to claim 59, wherein the cell comprises two or more of the at least one gene that codes for a fusion protein.

93 (previously presented). A process according to claim 59, wherein the cell comprises three or more of the at least one gene that codes for a fusion protein.

94 (previously presented). A process according to claim 59, wherein one or more of the surface-bound proteins are removed from the polymer particles.

95 (previously presented). A process according to claim 59, wherein the composition consists essentially of polymer particles having surface-bound proteins.

96 (withdrawn). A pharmaceutical preparation, pesticide or herbicide comprising polymer particles produced by a method according to claim 59.

REHM
Appl. No. 10/525,955
April 14, 2008

97 (previously presented). A method of binding a second biologically active substance comprising

A) providing a composition of polymer particles produced by a method according to claim 59, wherein optionally a coupling reagent is bound to the binding domain when a binding domain is present, and

B) contacting the composition with a sample comprising a second biologically active substance so that the binding domain or the biologically active protein or the coupling reagent binds the second biologically active substance.

98 (previously presented). A method according to claim 97, wherein the second biologically active substance is an oligopeptide, enzyme, abzyme, noncatalytic protein or antibody.

99 (canceled).

100 (new). A process according to claim 59, wherein the cell further comprises at least one gene that codes for an additional fusion protein, the additional fusion protein comprising

- (a) a polymer particle binding domain, or
 - (b) a protein involved in the formation of the polymer particles, the protein comprising a polymer particle binding domain,
- the additional fusion protein further comprising
- (i) at least one biologically active protein, or

REHM

Appl. No. 10/525,955

April 14, 2008

(ii) at least one binding domain capable of binding one or more biologically active substances or one or more coupling reagents, or

(iii) at least one biologically active protein and at least one binding domain capable of binding one or more biologically active substances or one or more coupling reagents, or

(iv) a combination thereof.